

Figure 1

fraction: M L 21 22 23 24 25 26 27 28 29 30 31 32

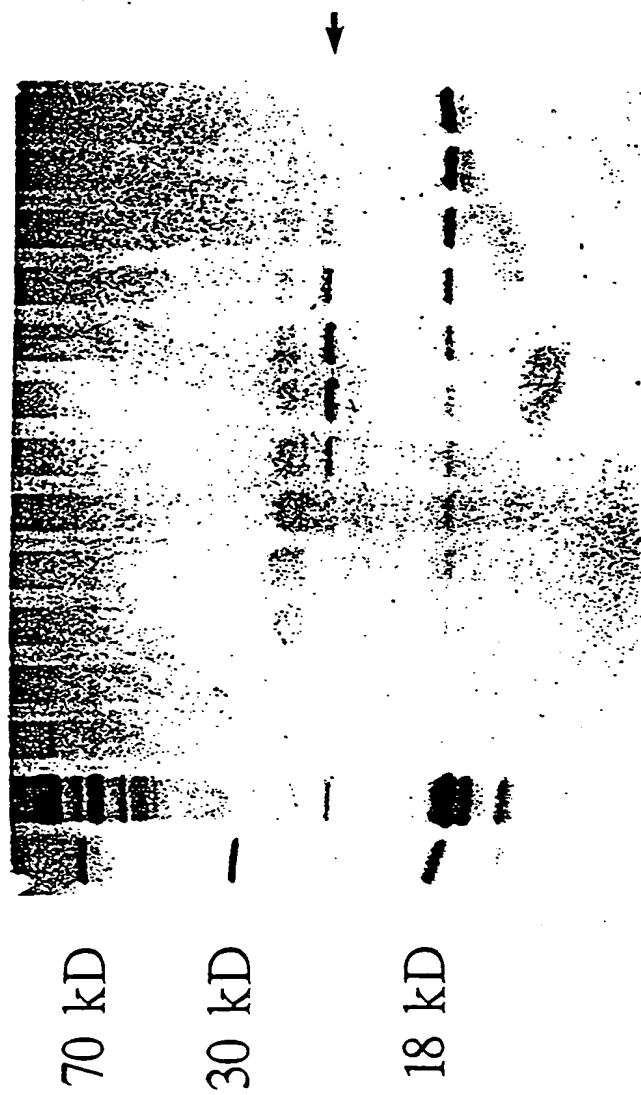


Figure 2a

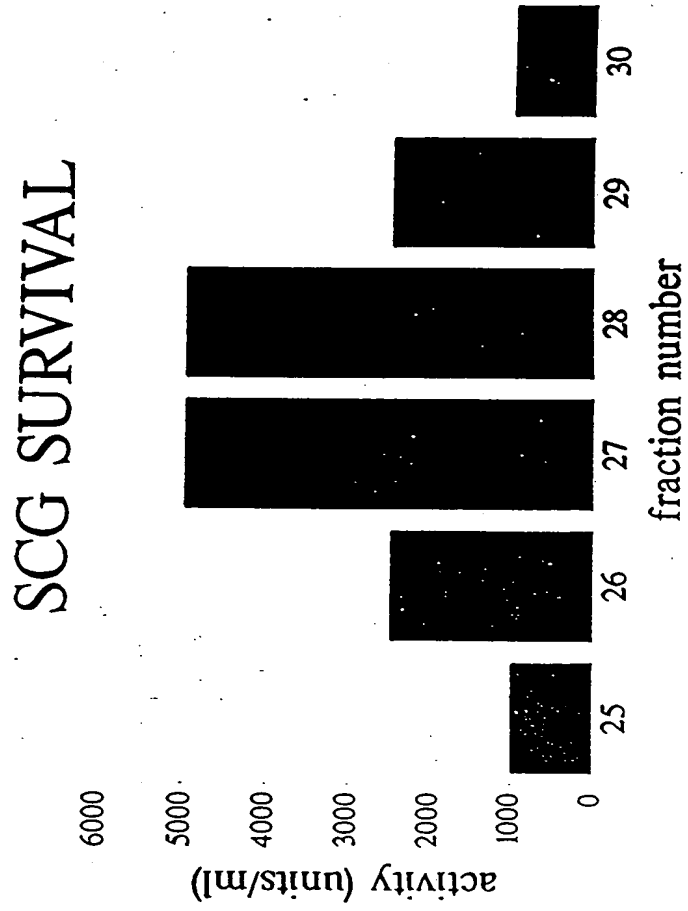


Figure 2b

Figure 3a NGF

Figure 3b Anti-NGF



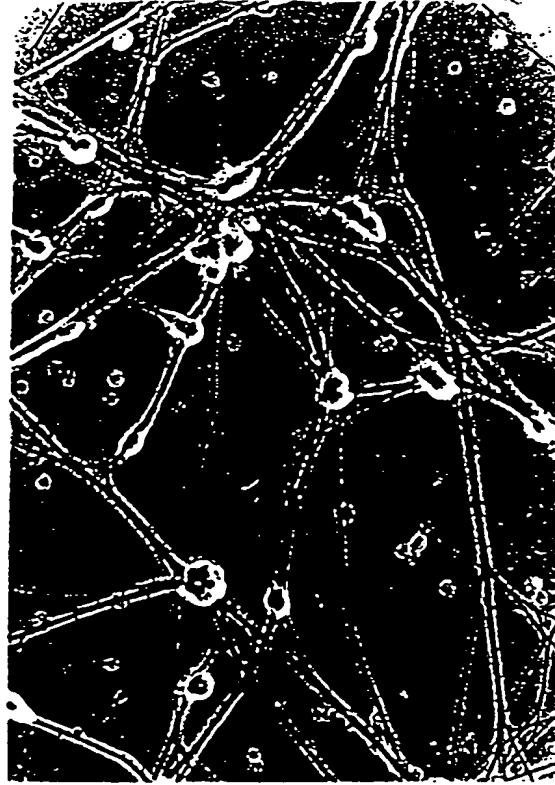
[illegible]

Figure 3c Anti-NGF
+
Neurturin

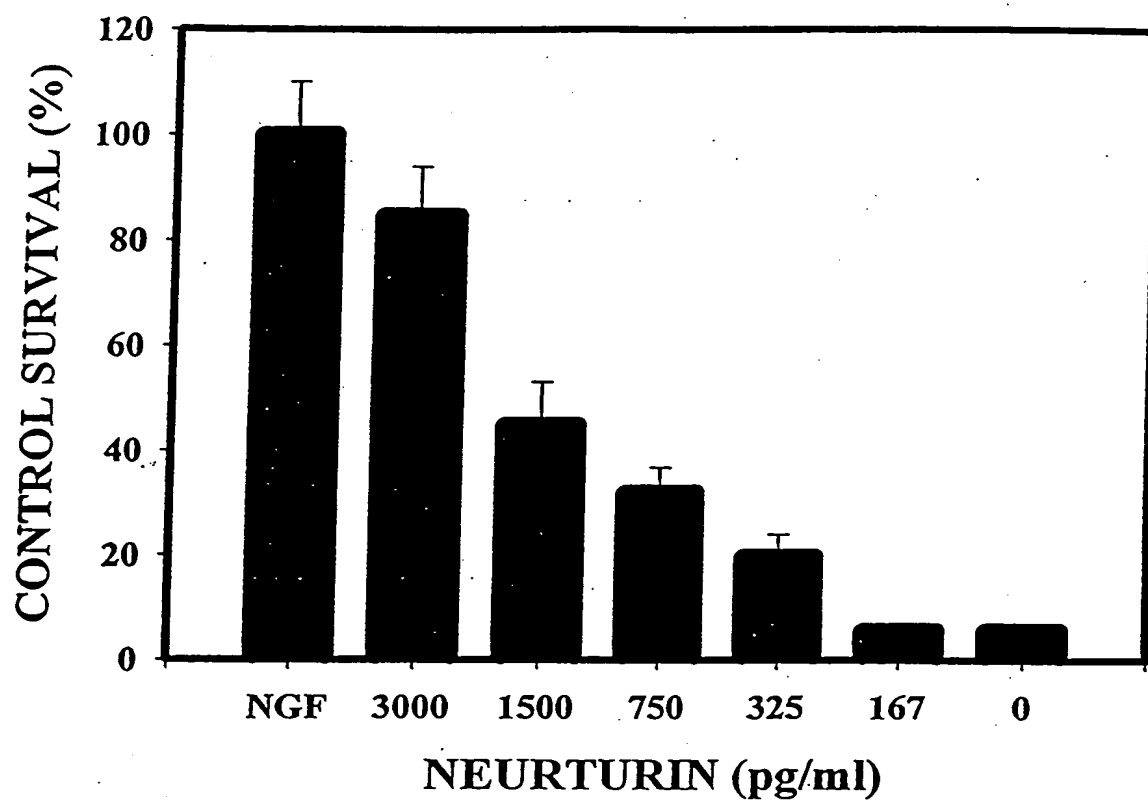


Figure 4

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------|---|---|---|---|---|---|---|---|---|---|---|---|------|-------|------|
| 1 | S | P | D | K | Q | H | A | V | L | P | R | R | E | R | N | R | Q | A | A | A | A | N | P | E | N | S | R | G | K | G | hGDNF | |
| 1 | S | P | D | K | Q | A | A | A | L | P | R | R | E | R | N | R | Q | A | A | A | A | S | P | E | N | S | R | G | K | G | mGDNF | |
| 1 | S | P | D | K | Q | A | A | A | L | P | R | R | E | R | N | R | Q | A | A | A | A | S | P | E | N | S | R | G | K | G | rGDNF | |
| 1 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | hNTN | |
| 1 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | mNTN | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 31 | R | R | G | Q | R | G | K | N | R | G | C | V | L | T | A | I | H | L | N | V | T | D | L | G | L | G | Y | E | T | K | hGDNF | |
| 31 | R | R | G | Q | R | G | K | N | R | G | C | V | L | T | A | I | H | L | N | V | T | D | L | G | L | G | Y | E | T | K | mGDNF | |
| 31 | R | R | G | Q | R | G | K | N | R | G | C | V | L | T | A | I | H | L | N | V | T | D | L | G | L | G | Y | E | T | K | rGDNF | |
| 1 | - | - | - | - | A | R | L | G | A | R | P | C | G | L | R | E | L | E | V | R | V | S | E | L | G | L | G | Y | A | S | D | hNTN |
| 1 | - | - | - | - | P | G | A | R | P | C | G | L | R | E | L | E | V | R | V | S | E | L | G | L | G | Y | T | S | D | mNTN | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 61 | E | E | L | I | F | R | Y | C | S | G | S | C | D | A | A | E | T | T | Y | D | K | I | L | K | N | L | S | R | N | R | hGDNF | |
| 61 | E | E | L | I | F | R | Y | C | S | G | S | C | E | S | A | E | T | M | Y | D | K | I | L | K | N | L | S | R | S | R | mGDNF | |
| 61 | E | E | L | I | F | R | Y | C | S | G | S | C | E | A | A | E | T | M | Y | D | K | I | L | K | N | L | S | R | S | R | rGDNF | |
| 28 | E | T | V | L | F | R | Y | C | A | G | A | C | E | A | A | A | R | V | Y | D | L | G | L | R | R | L | R | Q | R | R | hNTN | |
| 26 | E | T | V | L | F | R | Y | C | A | G | A | C | E | A | A | I | R | I | Y | D | L | G | L | R | R | L | R | Q | R | R | mNTN | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 91 | R | L | V | S | D | K | V | - | G | Q | A | C | C | R | P | I | A | F | D | D | D | L | S | F | L | D | D | N | L | V | hGDNF | |
| 91 | R | L | T | S | D | K | V | - | G | Q | A | C | C | R | P | V | A | F | D | D | D | L | S | F | L | D | D | N | L | V | mGDNF | |
| 91 | R | L | T | S | D | K | V | - | G | Q | A | C | C | R | P | V | A | F | D | D | D | L | S | F | L | D | D | S | L | V | rGDNF | |
| 58 | R | L | R | R | E | R | V | R | A | Q | P | C | C | R | P | T | A | Y | E | D | E | V | S | F | L | D | A | H | S | R | hNTN | |
| 56 | R | V | R | R | E | R | A | R | A | H | P | C | C | R | P | T | A | Y | E | D | E | V | S | F | L | D | V | H | S | R | mNTN | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 120 | Y | H | I | L | R | K | H | S | A | K | R | C | G | C | I | - | hGDNF | | | | | | | | | | | | | | | |
| 120 | Y | H | I | L | R | K | H | S | A | K | R | C | G | C | I | - | mGDNF | | | | | | | | | | | | | | | |
| 120 | Y | H | I | L | R | K | H | S | A | K | R | C | G | C | I | - | rGDNF | | | | | | | | | | | | | | | |
| 88 | Y | H | T | V | H | E | L | S | A | R | E | C | A | C | V | - | hNTN | | | | | | | | | | | | | | | |
| 86 | Y | H | T | L | Q | E | L | S | A | R | E | C | A | C | V | - | mNTN | | | | | | | | | | | | | | | |

Figure 5

RT-PCR Analysis of Neurturin and GDNF

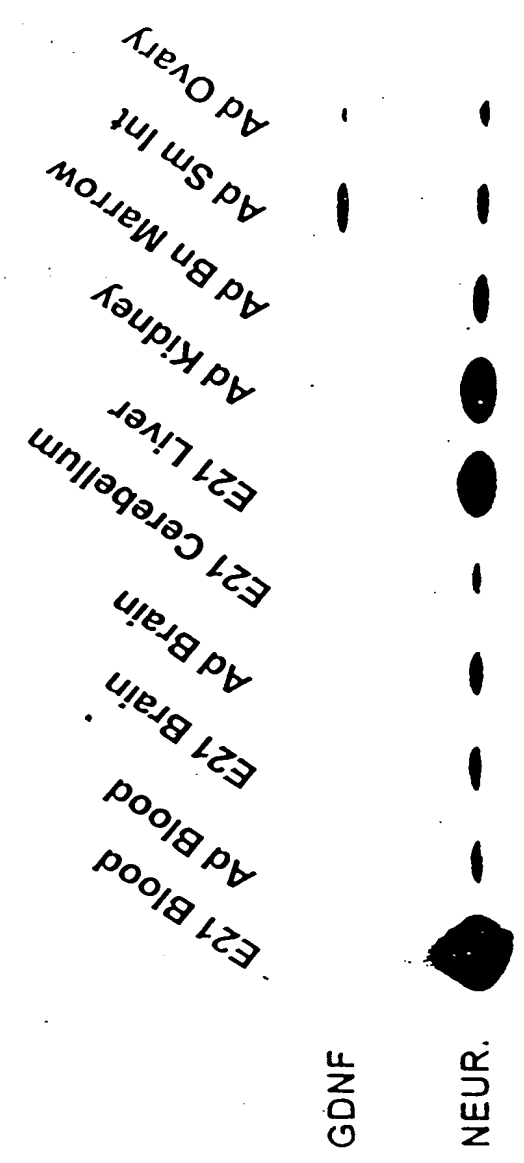


Figure 6

ATGCAGCGCTGGAAGGCGGCGGCCTTGGCCTCAGTGCTCTGCAGCTCCGTGCTGTCCATC 60
Met Gln Arg Trp Lys Ala Ala Ala Leu Ala Ser Val Leu Cys Ser Ser Val Leu Ser Ile
 TGGATGTGTGCGAGAGGGCCTGCTTCTCAGCCACCGCCTCGGACCTGCGCTGGTCCCCTG 120
Trp Met Cys Arg Glu Gly Leu Leu Leu Ser His Arg Leu Gly Pro Ala Leu Val Pro Leu
 CACCGCCTGCCTCGAACCCTGGACGCCCGGATTGCCCGCCTGGCCAGT⁺ACCGTGCACTC 180
His Arg Leu Pro Arg Thr Leu Asp Ala Arg Ile Ala Arg Leu Ala Gln Tyr Arg Ala Leu
 CTGCAGGGGGCCCCGGATGCGATGGAGCTGCGCGAGCTGACGCCCTGGGCTGGGCGGCCCC 240
Leu Gln Gly Ala Pro Asp Ala Met Glu Leu Arg Glu Leu Thr Pro Trp Ala Gly Arg Pro
 CCAGGTCCGCGCCGTGCGGCGGGGCCCCGGCGGCGGCGCGCGCTGCGCGGTTGGGGGCG 300
Pro Gly Pro Arg Arg Arg Ala Gly Pro Arg Arg Arg Ala Arg Ala Arg Leu Gly Ala
 CGGCCTTGCGGGCTGCGCGAGCTGGAGGTGCGCGTGAGCGAGCTGGGCCTGGGCTACGCG 360
Arg Pro Cys Gly Leu Arg Glu Leu Glu Val Arg Val Ser Glu Leu Gly Leu Gly Tyr Ala
 TCCGACGAGACGGTGCTGTTCCGCTACTGCGCAGGCGCCTGCGAGGCTGCCGCGCGCGTC 420
Ser Asp Glu Thr Val Leu Phe Arg Tyr Cys Ala Gly Ala Cys Glu Ala Ala Ala Arg Val
 TACGACCTCGGGCTGCGACGACTGCGCCAGCGGCGGCGCCTGCGGCGGGAGCGGGTGCGC 480
Tyr Asp Leu Gly Leu Arg Arg Leu Arg Gln Arg Arg Arg Leu Arg Arg Glu Arg Val Arg
 GCGCAGCCCTGCTGCCGCCCGACGGCCTACGAGGACGAGGTGTCCTTCCTGGACGCGCAC 540
Ala Gln Pro Cys Cys Arg Pro Thr Ala Tyr Glu Asp Glu Val Ser Phe Leu Asp Ala His
 AGCCGCTACCACACGGTGACGAGCTGTCGGCGCGCGAGTGCGCCTGCGTGTGA 594
Ser Arg Tyr His Thr Val His Glu Leu Ser Ala Arg Glu Cys Ala Cys Val

Figure 7

ATGAGGCGCTGGAAGGCAGCGGCCCTGGTGTGCTCATCTGCAGCTCCCTGCTATCTGTC 60
Met Arg Arg Trp Lys Ala Ala Ala Leu Val Ser Leu Ile Cys Ser Ser Leu Leu Ser Val
 TGGATGTGCCAGGAGGGTCTGCTCTTGGGCCACCGCCTGGGACCCGCGCTTGCCCCGCTA 120
Trp Met Cys Gln Glu Gly Leu Leu Leu Gly His Arg Leu Gly Pro Ala Leu Ala Pro Leu
 CGACGCCCTCCACGCACCCTGGACGCCCCGATCGCCCGCTGGCCCAGTATCGCGCTCTG 180
Arg Arg Pro Pro Arg Thr Leu Asp Ala Arg Ile Ala Arg Leu Ala Gln Tyr Arg Ala Leu
 CTCCAGGGCGCCCCGACGCGGTGGAGCTTCGAGAACTTCTCCCTGGGCTGCCCCGATC 240
Leu Gln Gly Ala Pro Asp Ala Val Glu Leu Arg Glu Leu Ser Pro Trp Ala Ala Arg Ile
 CCGGGACCGCGCCGTCGAGCGGGTCCCCGGCGTCGGCGGGCGCGGCCGGGGGCTCGGCCT 300
Pro Gly Pro Arg Arg Arg Ala Gly Pro Arg Arg Arg Arg Ala Arg Pro Gly Ala Arg Pro
 TGTGGGCTGCGCGAGCTCGAGGTGCGCGTGAGCGAGCTGGGCCTGGGCTACACGTCGGAT 360
Cys Gly Leu Arg Glu Leu Glu Val Arg Val Ser Glu Leu Gly Leu Gly Tyr Thr Ser Asp
 GAGACCGTGCTGTTCCGCTACTGCGCAGGCGCGTGCGAGGCGGCCATCCGCATCTACGAC 420
Glu Thr Val Leu Phe Arg Tyr Cys Ala Gly Ala Cys Glu Ala Ala Ile Arg Ile Tyr Asp
 CTGGGCCTTCGGCGCCTGCGCCAGCGGAGGCGCGTGCGCAGAGAGCGGGCGCGGGCGCAC 480
Leu Gly Leu Arg Arg Leu Arg Gln Arg Arg Arg Val Arg Arg Glu Arg Ala Arg Ala His
 CCGTGTTGTCGCCCCGACGGCCTATGAGGACGAGGTGTCCTTCCTGGACGTGCACAGCCGC 540
Pro Cys Cys Arg Pro Thr Ala Tyr Glu Asp Glu Val Ser Phe Leu Asp Val His Ser Arg
 TACCACACGCTGCAAGAGCTGTGCGCGCGGGAGTGCGCGTGCGTGTGA 588
Tyr His Thr Leu Gln Glu Leu Ser Ala Arg Glu Cys Ala Cys Val

Figure 8

| | |
|--|------|
| GGAGGGAGAGCGCGCGGTGGTTTCGTCCGTGTGCCCCGCGCCCGGCGC | -301 |
| TCCTCGCGTGGCCCCGCGTCCTGAGCGCGCTCCAGCCTCCCACGCGCGCC | -251 |
| ACCCCGGGGTTCAGTGAAGCCGCGAGCCCGGGGAAGACAGAGAAAGAGA | -201 |
| GGCCAGGGGGGGAACCCCATGGCCCGGCGCGTGTCCCGCACCCCTGTGCGG | -151 |
| TGGCCTCCTCCGGCAAGGGGTCCCGGGTCCGCTCCGGTCCCGCGATCC | -101 |
| GGATGGCGCACGCAGTGGCTGGGGCCGGGCCGGGCTCGGGTGGTCGGAGG | -51 |
| AGTCAACCACTGACGGGTCACTCTGGAGCCCGTGGCAGGCCGAGGCCAGG | -1 |
| ATGAGGCGCTGGAAGGCAGCGGCCCTGGTGTGCTCATCTGCAGCTCCCT | 50 |
| <u>GCTATCTGTCTGGATGTGCCAGGAGGGTCTGCTCTTGGGCCACCGCCTGG</u> | 100 |
| <u>GACCCGCGCTTGCCCCGCTACGACGCCCTCCACGCACCCCTGGAAGCCCGC</u> | 150 |
| <u>ATCGCCCGCCTGGCCAGTATGCGCTCTGCTCCAGGGCGCCCCGAAGC</u> | 200 |
| <u>GGTGGAGCTTCGAGAACTTTCTCCCTGGGCTGCCCGCATCCCGGGACCGC</u> | 250 |
| <u>GCCGTGAGCGGGTCCCCGGCGTCGGCGGGCGCGGCCGGGGGCTCGGCCT</u> | 300 |
| <u>TGTGGGCTGCGGAGCTCGAGGTGCGCGTGAGCGAGCTGGGCCTGGGCTA</u> | 350 |
| <u>CACGTCCGATGAGACCGTGCTGTTCCGCTACTGCGCAGGCGCGTGCGAGG</u> | 400 |
| <u>CGGCCATCCGCATCTACGACCTGGGCCTTCGGGCGCTGCGCCAGCGGAGG</u> | 450 |
| <u>CGCGTGCGCAGAGAGCGGGCGCGGGCGCACCCGTGTTGTGCGCCGACGGC</u> | 500 |
| <u>CTATGAGGACGAGGTGTCCTTCCTGGACGTGCACAGCCGCTACCACAGC</u> | 550 |
| <u>TGCAAGAGCTGTGCGCGCGGGAGTGCGCGTGCGTGTGATGCTACCTCAG</u> | 600 |
| CCCCCGACCTGCGAAAGGGCCCTCCCTGCCGACCCTCGCTGAGAACTGA | 650 |
| CTTCACATAAAGTGTGGGAACTCCC | 675 |

Figure 9

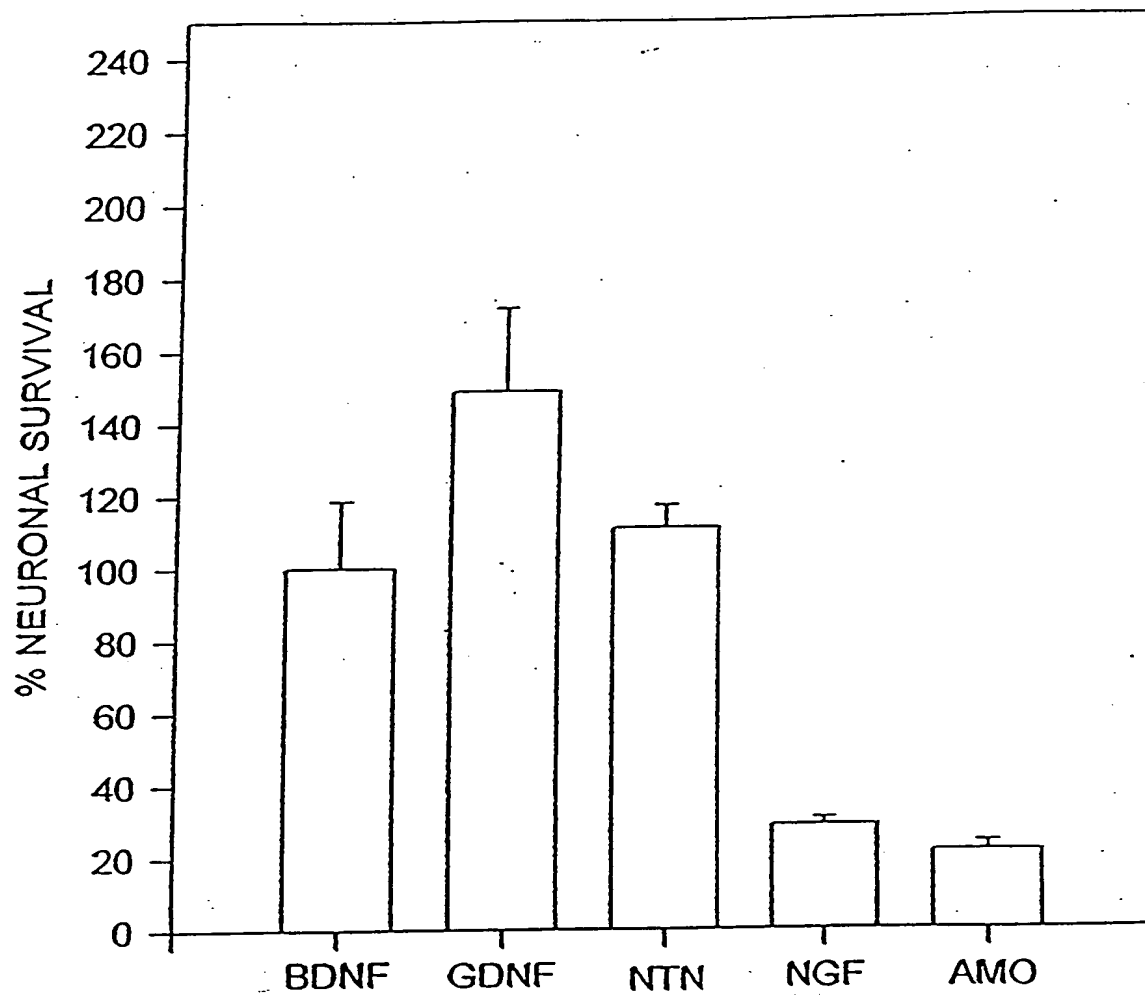


Figure 10

| | |
|---|-----|
| GAGGGACCTGGACGCCCCATCAGGGTAAGAATTCCTGGGGGCCTCCCGACTCCCCAATTC | 60 |
| Glu Gly Pro Gly Arg Pro Ile Arg Val Arg Ile Pro Gly Gly Leu Pro Thr Pro Gln Phe | 20 |
| CTTCTCTCAAAGCCCTCACTTTGCCTTACAATCCTACTCTACCTTGCACTAGGTAACAAC | 120 |
| Leu Leu Ser Lys Pro Ser Leu Cys Leu Thr Ile Leu Leu Tyr Leu Ala Leu Gly Asn Asn | 40 |
| CATGTCCGTCCTTCCAAGAGCCCTTGGCTGGTTCATGCCGACTGTGGAGCCTGACCCTACCA | 180 |
| His Val Arg Leu Pro Arg Ala Leu Ala Gly Ser Cys Arg Leu Trp Ser Leu Thr Leu Pro | 60 |
| GTGGCTGAGCTGGGCTGGGCTATGCCTCGGAGGAGAAGGTCATCTTCGATACTGTGCT | 240 |
| Val Ala Glu Leu Gly Leu Gly Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala | 80 |
| GGCAGCTGTCCCCAAGAGGCCCCGTACCCAGCACAGTCTGGTACTGGCCCCGGCTTCGAGGG | 300 |
| Gly Ser Cys Pro Gln Glu Ala Arg Thr Gln His Ser Leu Val Leu Ala Arg Leu Arg Gly | 100 |
| CGGGGTCGAGCCCATGGCCGACCCTGCTGCCAGCCCACCAGCTATGCTGATGTGACCTTC | 360 |
| Arg Gly Arg Ala His Gly Arg Pro Cys Cys Gln Pro Thr Ser Tyr Ala Asp Val Thr Phe | 120 |
| CTTGATGATCAGCACCATTTGGCAGCAGCTGCCTCAGCTCTCAGCTGCAGCTTGTGGCTGT | 420 |
| Leu Asp Asp Gln His His Trp Gln Gln Leu Pro Gln Leu Ser Ala Ala Ala Cys Gly Cys | 140 |
| GGTGGCTGAAGGAGGCCAGTCTGGTGTCTCAGAATCACAAGCATGAGACAGGCTGGGCTT | 480 |
| Gly Gly | 142 |
| TGAAAGGCTCAGGTGACATTACTAGAAATTTGCATAGGTAAAGATAAGAAGGGAAAGGAC | 540 |
| CAGG | 544 |

Figure 11

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----|------|
| 1 | C | V | L | T | A | I | H | L | N | V | T | D | L | G | L | G | Y | E | T | K | E | E | L | I | F | R | Y | C | S | G | S | C | E | - | S | A | E | T | M | Y | D | K | I | L | K | N | L | S | R | S | GDNF |
| 1 | C | G | L | R | E | L | E | V | R | V | S | E | L | G | L | G | Y | T | S | D | E | T | V | L | F | R | Y | C | A | G | A | C | E | A | A | I | R | I | - | Y | D | L | G | L | R | L | R | Q | R | NTN | |
| 1 | C | R | L | W | S | L | T | L | P | V | A | E | L | G | L | G | Y | A | S | E | E | K | V | I | F | R | Y | C | A | G | S | C | P | Q | E | A | R | T | Q | H | S | L | V | L | A | R | L | R | G | R | PSP |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|------|-----|
| 50 | R | R | L | T | S | O | K | V | - | G | Q | A | C | C | R | P | V | A | F | D | D | L | S | F | L | D | D | N | L | V | Y | H | I | L | R | K | H | S | A | K | R | C | G | C | I | GDNF | |
| 50 | R | R | V | R | R | E | R | A | R | A | H | P | C | C | R | P | T | A | Y | E | D | E | V | S | F | L | D | V | H | S | R | Y | H | T | L | Q | E | L | S | A | R | E | C | A | C | V | NTN |
| 51 | R | - | - | - | - | G | R | A | H | G | R | P | C | C | Q | P | T | S | Y | A | D | - | V | T | F | L | D | D | Q | H | H | W | Q | Q | L | P | Q | L | S | A | A | C | C | G | G | G | PSP |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|----|----|----|----|----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|------|-----|-----|
| 50 | RR | LT | SD | KV | - | G | Q | A | C | C | R | P | V | A | E | D | D | L | S | F | L | D | D | N | L | V | Y | H | I | L | R | K | H | S | A | K | R | C | G | C | I | . | GDNF | | |
| 50 | RR | V | R | R | E | R | A | H | P | C | C | R | P | T | A | E | D | E | V | S | F | L | D | V | H | S | R | Y | H | T | L | Q | E | L | S | A | R | E | C | A | C | V | : | NTN | |
| 51 | - | - | - | - | - | G | R | A | H | G | R | P | C | C | Q | P | T | S | A | D | - | V | T | F | L | D | D | Q | H | H | W | Q | L | P | Q | L | S | A | A | C | G | C | G | . | PSP |

CCTCAGAGGAGAAGATTATCTTCCGATACTGTGCTGGCAGCTGTCCCCAAGAGGTCCGTACC 62
 Ser Glu Glu Lys Ile Ile Phe Arg Tyr Cys Ala Gly Ser Cys Pro Gln Glu Val Arg Thr 20

CAGCACAGTCTGGTGCTGGCCCCGTCTTCGAGGGCAGGGTCGAGCTCATGGCAGACCTTGC 122
 Gln His Ser Leu Val Leu Ala Arg Leu Arg Gly Gln Gly Arg Ala His Gly Arg Pro Cys 40

TGCCAGCCCACCAGCTATGCTGATGTGACCTTCCTTGATGACCACCACCATTGGCAGCAG 182
 Cys Gln Pro Thr Ser Tyr Ala Asp Val Thr Phe Leu Asp Asp His His His Trp Gln Gln 60

CTGCCTCAGCTCTCAGCCGCAGCTTGTGGCTGTGGTGGCTGAAGGCGGCCAGCCTGGTCT 242
 Leu Pro Gln Leu Ser Ala Ala Ala Cys Gly Cys Gly Gly 73

CTCAGAATCACAAGCAAGAGGCAGCCTTTGAAAGGCTCAGGTGACGTTATTAGAAACTTG 302

CATAGGAGAAGATTAAGAAGAGAAAGGGGACCTG 336

Figure 13

| | |
|---|-----|
| TGCCGGCTGTGGAGCCTGACCCTACCAGTGGCTGAGCTTGGCCTGGGCTATGCCTCAGAG | 60 |
| Cys Arg Leu Trp Ser Leu Thr Leu Pro Val Ala Glu Leu Gly Leu Gly Tyr Ala Ser Glu | 20 |
| GAGAAGATTATCTTCCGATACTGTGCTGGCAGCTGTCCCAAGAGGTCCGTACCCAGCAC | 120 |
| Glu Lys Ile Ile Phe Arg Tyr Cys Ala Gly Ser Cys Pro Gln Glu Val Arg Thr Gln His | 40 |
| AGTCTGGTGCTGGCCCGTCTTCGAGGGCAGGGTCGAGCTCATGGCAGACCTTGCTGCCAG | 180 |
| Ser Leu Val Leu Ala Arg Leu Arg Gly Gln Gly Arg Ala His Gly Arg Pro Cys Cys Gln | 60 |
| CCCACCAGCTATGCTGATGTGACCTTCCTTGATGACCACCACCATTGGCAGCAGCTGCCT | 240 |
| Pro Thr Ser Tyr Ala Asp Val Thr Phe Leu Asp Asp His His His Trp Gln Gln Leu Pro | 80 |
| CAGCTCTCAGCCGCAGCTTGTTGGCTGTGGTGGCTGAAGGCGGCCAGCCTGGTCTCTCAGA | 300 |
| Gln Leu Ser Ala Ala Ala Cys Gly Cys Gly Gly | 91 |
| ATCACAAGCAAGAGGCAGCCTTTGAAAGGCTCAGGTGACGTTATTAGAACTTGTCATAGG | 360 |
| AGAAGATTAAGAAGAGAAAGGGGACCTGATT | 391 |

Figure 14

| | 10 | 20 | 30 | |
|----|---|----|----|------|
| 1 | A L A G S C R L W S L T L P V A E L G L G Y A S E E K V I F | | | mPSP |
| 1 | A L P G L C R L W S L T L P V A E L G L G Y A S E E K I I F | | | rPSP |
| 1 | A L S G P C Q L W S L T L S V A E L G L G Y A S E E K V I F | | | hPSP |
| 31 | R Y C A G S C C P Q E A R T Q H S L V L A R L R G R G R A H G | 50 | 60 | mPSP |
| 31 | R Y C A G S C C P Q E V R T Q H S L V L A R L R G Q G R A H G | | | rPSP |
| 31 | R Y C A G S C C P R G A R T Q H G L A L A R L Q G Q G R A H G | | | hPSP |
| 61 | R P C C Q P T S Y A D V T F L D D D Q H H W Q Q L P Q L S A A | 80 | 90 | mPSP |
| 61 | R P C C Q P T S Y A D V T F L D D D H H W Q Q L P Q L S A A | | | rPSP |
| 61 | G P C C R P T R Y T D V A F L D D D R H R W Q R L P Q L S A A | | | hPSP |
| 91 | A C G C C G G | | | rPSP |
| 91 | A C G C C G G | | | rPSP |
| 91 | A C G C C G G | | | hPSP |

Figure 15B

| EO | D | GROWTH | 0: | FACTOR | SEQUENCE |
|----|--------|--------|----|--------|--|
| 50 | TGFβ1 | | | | CCVRLYIDFRKDLGWK-WIHEPKGYHANFCLGPCPYINSLDT-----QYSKVLALYNQHNPGASAA-PCCV--POALEPLPIVYVGRKPKV--EQLSNMIVRSCKCS |
| 51 | TGFβ2 | | | | CCLRLYIDFRKDLGWK-WIHEPKGYANANFCAGACPYLWSSDT-----QHSRLSLYNTINPEASAS-PCCV--SQDLEPLTILYIGKTPKI--EQLSNMIVKSCCKCS |
| 52 | TGFβ3 | | | | CCVRLYIDFRKDLGWK-WIHEPKGYANFCGSGPCPYLRSADT-----THSTVLGLYNTLNPEASAS-PCCV--PQDLEPLTILYVGRTPKV--EQLSNMIVKSCCKCS |
| 53 | INH8A | | | | CKKOFFVSFK-DIGWQDWIIAPSGYHANYCEGECPSHLAG-TSGSSLSFHSVTINHYMRGHSFANLKSCCV--PTKLRPMMLYDDGQNI--KKDIQNMIVEECGCS |
| 54 | INH8B | | | | CCROOFFIDFR-LIGWQDWIIAPTGYGNYCEGSCPAYLAG-VPGSASSFHTAVNQYMRGLNP-GTVNSCCI--PTKLSTMSMLYDDEYNIV-KRDVPNMIVEECGCA |
| 55 | NODAL | | | | CRRVKFQVDEN-LIGWQDWIIYPKQYNAIRCEGECNPVGEFHPT-----NHAYIOSLLKRYQPHR-VPSTCCA--PVKTKPLSMLYDNGR--VLEHKKDMIVEECGCL |
| 56 | BMP2 | | | | CKRHPLYVDFS-DVGWQDWIVAPPGYHAFYCHGECFPPLADHLNST-----NHAIVQTLWSVNS-K-IPKACCV--PTELSAISMLYDENEKVLK-NYQDMVVEGCGCR |
| 57 | BMP4 | | | | CRRHSLYVDFS-DVGWQDWIVAPPGYQAFYCHGDCFPPLADHLNST-----NHAIVQTLWSVNS-S-IPKACCV--PTELSAISMLYDDEYDKWLK-NYQEMVVEGCGCR |
| 58 | DPP | | | | CRRHSLYVDFS-DVGWQDWIVAPLGYDAYYCHGCKCFPLADHFNST-----NHAIVQTLVNMNPGK-VPKACCV--PTQLDSVAMLYLNDQSTWLK-NYQEMTVVGGCGR |
| 59 | BMP5 | | | | CKKHLYVSFR-DLGWQDWIIAPEGYAAFYCDGECFPLNAHMNAT-----NHAIVQTLVHLMFPH-VPKPCCA--PTKLNAISVLYFDDSSNVILK-KYRNMVVRSCGCH |
| 60 | BMP6 | | | | CRKHLYVSFQ-DLGWQDWIIAPKGYAANYCDGECFPLNAHMNAT-----NHAIVQTLVHLMNPEY-VPKPCCA--PTKLNAISVLYFDDNSNVILK-KYRNMVVRACGCH |
| 61 | BMP7 | | | | CKKHLYVSFR-DLGWQDWIIAPEGYAAAYCEGECFPLNSYMNAT-----NHAIVQTLVHFINPET-VPKPCCA--PTQLNAISVLYFDDSSNVILK-KYRNMVVRACGCH |
| 62 | BMP8 | | | | CRRHLYVSFQ-DLGWLDWVIAPOGYSAYYCEGECFPLDSCMNAT-----NHAIVQTLVHLMKPN-VPKACCA--PTKLNAISVLYFDDSSNVILK-KYRNMVVRACGCH |
| 63 | 60A | | | | CMQOTLYIDFK-DLGWHDWIIAPEGYAFYCSGECNCFPLNAHMNAT-----NHAIVQTLVHLEPKK-VPKPCCA--PTKLNAISVLYFDDSSNVILK-KYRNMVVRACGCH |
| 64 | BMP3 | | | | CARRYLVDFDA-DIGWSEWIIISPKSFDAYYCSGACQFPMPSLKPS-----NHAIVQTLVHLMNPEY-VPKPCCA--PTKLNAISVLYFDDSSNVILK-KYRNMVVRACGCH |
| 65 | VG1 | | | | CKKRHLVVEFK-DVGWQDWVIAPOGYMANYCYGECFPLTEILNGS-----NHAIVQTLVHLMNPEY-VPKPCCA--PTKLNAISVLYFDDSSNVILK-KYRNMVVRACGCH |
| 66 | GDF1 | | | | CRARLLVVSFR-EVGWHRWVIAPRGFLANYCQGCALPVASGSGGPPALNHAIVRALMHAAAPGA-ADLPCCV--PTKMSPIISMLFYDNDNVILK-HYENMAVDECGCR |
| 67 | GDF3 | | | | CHRHOLFNFQ-DLGWQDWVIAPOGYMANYCHGECFPMPTTLNNS-----NYAFMOALMHMADP-K-VPKACCV--PTKLNAISVLYFDDSSNVILK-HYEDMVVDECGCR |
| 68 | DORSLN | | | | CRRTSLVNFK-EIGWDSWIIAPKDYEAFCCKGGCFPLTDNVPT-----KHAIVQTLVHLMNPEY-VPKPCCA--PTKLNAISVLYFDDSSNVILK-HYEDMVVDECGCR |
| 69 | INHα | | | | CHRVALLNFS-QELGWERWIVYPPSFIHYCHGGGLHIPPNSLPVPGAPPTPAQPSYLL-----PGAQPCCAALPGTMRPLHVRTTSDGGYSFKYETVPLNLTQHCACI |
| 70 | MIS | | | | CALRELSVDLRAERS-----VLIPETYQANNCQAGCWQSDR-----NPRYGNHVVLLKMQARGATLARPCCV--PTAYT--GKLLISLSEERISAHVPMNVAETECGR |
| 71 | GDF9 | | | | CELHDFSLSFS-QLKWDNWIVAPHSYNPSYCKGDCPSAVSHRYGSPV-----HTMWQNMIEY-KLDPSVPSPCV--PGKYSPLSVLTIEPDGSIAYK-EYEDMMATSTCTCR |
| 72 | GDNF | | | | CVLTAIHLNVT-DLGLG--YETKEELIFRYCSGSCD-AAETTYDKILKLSRN-----RRLVSDKV-GQACCRPIAFD-DDLSFL-----DDNLVYHILRKHSKRCGCI |
| 73 | NTN | | | | CGLRELEVRVS-ELGLG--YASDETIVLFRYCAGACE-AAARVYDLGLRLRQR-----RRLRRERVRAQPCCRPTAYE-DEVSL-----DAHSRYHTVHLSARECACV |

FIGURE 16

| | | | | | | |
|-----|------------|------------|-------------|------------|------------|------------|
| 1 | ATGGCTGCAG | GAAGACTTCG | GATCCTGTGT | CTGCTGCTCC | TGTCCTTGCA | CCCGAGCCTC |
| | TACCGACGTC | CTTCTGAAGC | CTAGGACACA | GACGACGAGG | ACAGGAACGT | GGGCTCGGAG |
| 61 | GGCTGGGTCC | TTGATCTTCA | AGAGGCTTCT | GTGGCAGATA | AGCTCTCATT | TGGGAAGATG |
| | CCGACCCAGG | AACTAGAAGT | TCTCCGAAGA | CACCGTCTAT | TCGAGAGTAA | ACCCTTCTAC |
| | | | | ↓ | | |
| 121 | GCAGAGACTA | GAGGGACCTG | GACGCCCCAT | CAGGGTAAGA | ATTCCTGGGG | GCCTCCCGAC |
| | CGTCTCTGAT | CTCCCTGGAC | CTGCGGGGTA | GTCCCATTCT | TAAGGACCCC | CGGAGGGCTG |
| 181 | TCCCCAATTC | CTTCTCTCAA | AGCCCTCACT | TTGCCTTACA | ATCCTACTCT | ACCTTGCACT |
| | AGGGGTTAAG | GAAGAGAGTT | TCGGGAGTGA | AACGGAATGT | TAGGATGAGA | TGGAACGTGA |
| | ↓ | | | | | |
| 241 | AGGTAACAAC | CATGTCCGTC | TTCCAAGAGC | CTTGGCTGGT | TCATGCCGAC | TGTGGAGCCT |
| | TCCATTGTTG | GTACAGGCAG | AAGGTTCTCG | GAACCGACCA | AGTACGGCTG | ACACCTCGGA |
| 301 | GACCCTACCA | GTGGCTGAGC | TGGGCCTGGG | CTATGCCTCG | GAGGAGAAGG | TCATCTTCCG |
| | CTGGGATGGT | CACCGACTCG | ACCCGGACCC | GATACGGAGC | CTCCTCTTCC | AGTAGAAGGC |
| 361 | ATACTGTGCT | GGCAGCTGTC | CCCAAGAGGC | CCGTACCCAG | CACAGTCTGG | TACTGGCCCG |
| | TATGACACGA | CCGTCGACAG | GGGTCTCTCCG | GGCATGGGTC | GTGTCAGACC | ATGACCGGGC |
| 421 | GCTTCGAGGG | CGGGGTCGAG | CCCATGGCCG | ACCCTGCTGC | CAGCCCACCA | GCTATGCTGA |
| | CGAAGCTCCC | GCCCCAGCTC | GGGTACCGGC | TGGGACGACG | GTCGGGTGGT | CGATACGACT |
| 481 | TGTGACCTTC | CTTGATGATC | AGCACCATTG | GCAGCAGCTG | CCTCAGCTCT | CAGCTGCAGC |
| | ACACTGGAAG | GAAGTACTAG | TCGTGGTAAC | CGTCGTCGAC | GGAGTCGAGA | GTCGACGTCG |
| 541 | TTGTGGCTGT | GGTGGCTGAA | GGAGGCCAGT | CTGGTGTCTC | AGAATCACAA | GCATGAGACA |
| | AACACCGACA | CCACCGACTT | CCTCCGGTCA | GACCACAGAG | TCTTAGTGTT | CGTACTCTGT |
| 601 | GGCTGGGCTT | TGAAAGGCTC | AGGTGACATT | ACTAGAAATT | TGCATAGGTA | AAGATAAGAA |
| | CCGACCCGAA | ACTTTCCGAG | TCCACTGTAA | TGATCTTTAA | ACGTATCCAT | TTCTATTCTT |
| 661 | GGGAAAGGAC | CAGGGGTTTT | TTGTTTCTTT | CTTTGCTTGC | TTGTTAGTTT | TTTTTTTTTT |
| | CCCTTTCCTG | GTCCCCAAAA | AACAAAGAAA | GAAACGAACG | AACAATCAAA | AAAAAAAAAA |
| 721 | TTT | | | | | |
| | AAA | | | | | |

Figure 17A

| | | | | | | |
|-----|------------|-------------|------------|-------------|------------|-------------|
| 1 | ATGGCTGCAG | GAAGACTTCG | GATCCTGTGT | CTGCTGCTCC | TGTCCTTGCA | CCCGAGCCTC |
| | TACCGACGTC | CTTCTGAAGC | CTAGGACACA | GACGACGAGG | ACAGGAACGT | GGGCTCGGAG |
| 1 | M A A G | R L R | I L C | L L L L | S L H | P S L |
| 61 | GGCTGGGTCC | TTGATCTTCA | AGAGGCTTCT | GTGGCAGATA | AGCTCTCATT | TGGGAAGATG |
| | CCGACCCAGG | AACTAGAAGT | TCTCCGAAGA | CACCGTCTAT | TCGAGAGTAA | ACCCTTCTAC |
| 21 | G W V / L | D L Q | E A S | V A D K | L S F | G K M |
| | | | | ↓ | | |
| 121 | GCAGAGACTA | GAGGGACCTG | GACGCCCCAT | CAGGGTAACA | ACCATGTCCG | TCTTCCAAGA |
| | CGTCTCTGAT | CTCCCTGGAC | CTGCGGGGTA | GTCCCATTGT | TGGTACAGGC | AGAAGGTTCT |
| 41 | A E T R | G T W | T P H | Q G N N | H V R | L P R |
| 181 | GCCTTGCGTG | GTTTCATGCCG | ACTGTGGAGC | CTGACCCCTAC | CAGTGGCTGA | GCTGGGCGCTG |
| | CGGAACCGAC | CAAGTACGGC | TGACACCTCG | GACTGGGATG | GTCACCGACT | CGACCCGGAC |
| 61 | A L A G | S C R | L W S | L T L P | V A E | L G L |
| 241 | GGCTATGCCT | CGGAGGAGAA | GGTCATCTTC | CGATACTGTG | CTGGCAGCTG | TCCCCAAGAG |
| | CCGATACGGA | GCCTCCTCTT | CCAGTAGAAG | GCTATGACAC | GACCGTCGAC | AGGGGTTCTC |
| 81 | G Y A S | E E K | V I F | R Y C A | G S C | P Q E |
| 301 | GCCCGTACCC | AGCACAGTCT | GGTACTGGCC | CGGCTTCGAG | GGCGGGGTCG | AGCCCATGGC |
| | CGGGCATGGG | TCGTGTCAGA | CCATGACCGG | GCCGAAGCTC | CCGCCCCAGC | TCGGGTACCG |
| 101 | A R T Q | H S L | V L A | R L R G | R G R | A H G |
| 361 | CGACCCTGCT | GCCAGCCAC | CAGCTATGCT | GATGTGACCT | TCCTTGATGA | TCAGCACCAT |
| | GCTGGGACGA | CGGTCGGGTG | GTCGATACGA | CTACACTGGA | AGGAACTACT | AGTCGTGGTA |
| 121 | R P C C | Q P T | S Y A | D V T F | L D D | Q H H |
| 421 | TGGCAGCAGC | TGCCTCAGCT | CTCAGCTGCA | GCTTGTGGCT | GTGGTGGCTG | A |
| | ACCGTCGTCG | ACGGAGTCGA | GAGTCGACGT | CGAACACCGA | CACCACCGAC | T |
| 141 | W Q Q L | P Q L | S A A | A C G C | G G | |

Figure 17B

| | | | | | | |
|-----|------------|-------------|-------------|------------|-------------|------------|
| 1 | ATGGCTGCAG | GAAGACTTCG | GATCTTGTTT | CTGCTGCTCC | TGTCCTTGCA | CCTGGGCCTT |
| | TACCGACGTC | CTTCTGAAGC | CTAGAACAAA | GACGACGAGG | ACAGGAACGT | GGACCCGGAA |
| 61 | GGCTGGGTCC | TTGATCTTCA | AGAGGCTCCT | GCGGCAGATG | AGCTCTCATC | TGGGAAAATG |
| | CCGACCCAGG | AAC TAGAAGT | TCTCCGAGGA | CGCCGTCTAC | TCGAGAGTAG | ACCCTTTTAC |
| 121 | GCAGAGACTG | GAAGGACCTG | GAAGCCCCAT | CAGGGTAAGA | ATTCTTG GGG | GCCTCCTAAC |
| | CGTCTCTGAC | CTTCCTGGAC | CTTCGGGGTA | GTCCCATTCT | TAAGAACCCC | CGGAGGATTG |
| 181 | TCTACAGTTC | TTCCTCTCAA | AGCCCTCACT | TTGCCTCACA | ATCCTATTCT | ACCTTGCACT |
| | AGATGTCAAG | AAGGAGAGTT | TCGGGAGTGA | AACGGAGTGT | TAGGATAAGA | TGGAACGTGA |
| 241 | AGGTAACAAC | AATGTCCGCC | TTCCAAGAGC | CTTACCTGGT | TTGTGCCGGC | TGTGGAGCCT |
| | TCCATTGTTG | TTACAGGCGG | AAGGTTCTCG | GAATGGACCA | AACACGGCCG | ACACCTCGGA |
| 301 | GACCCTACCA | GTGGCTGAGC | TTGGCCTGGG | CTATGCCTCA | GAGGAGAAGA | TTATCTTCCG |
| | CTGGGATGGT | CACCGACTCG | AACCGGACCC | GATACGGAGT | CTCCTCTTCT | AATAGAAGGC |
| 361 | ATACTGTGCT | GGCAGCTGTC | CCCAAGAGGT | CCGTACCCAG | CACAGTCTGG | TGCTGGCCCG |
| | TATGACACGA | CCGTCGACAG | GGGTTCTCCA | GGCATGGGTC | GTGTCAGACC | ACGACCGGGC |
| 421 | TCTTCGAGGG | CAGGGTCGAG | CTCATGGCAG | ACCTTGCTGC | CAGCCCACCA | GCTATGCTGA |
| | AGAAGCTCCC | GTCCCAGCTC | GAGTACCGTC | TGGAACGACG | GTCGGGTGGT | CGATACGACT |
| 481 | TGTGACCTTC | CTTGATGACC | ACCACCAT TG | GCAGCAGCTG | CCTCAGCTCT | CAGCCGCAGC |
| | AACTGGAAG | GA ACTACTGG | TGGTGGTAAC | CGTCGTCGAC | GGAGTCGAGA | GTCGGCGTCG |
| 541 | TTGTGGCTGT | GGTGGCTGA | | | | |
| | AACACCGACA | CCACCGACT | | | | |

Figure 18A

| | | | | | | |
|-----|------------|------------|------------|------------|------------|------------|
| 1 | ATGGCTGCAG | GAAGACTTCG | GATCTTGTTT | CTGCTGCTCC | TGTCCTTGCA | CCTGGGCCTT |
| | TACCGACGTC | CTTCTGAAGC | CTAGAACAAA | GACGACGAGG | ACAGGAACGT | GGACCCGGAA |
| 1 | M A A G | R L R | I L F | L L L L | S L H | L G L |
| 61 | GGCTGGGTCC | TTGATCTTCA | AGAGGCTCCT | GCGGCAGATG | AGCTCTCATC | TGGGAAAATG |
| | CCGACCCAGG | AACTAGAAGT | TCTCCGAGGA | CGCCGTCTAC | TCGAGAGTAG | ACCCTTTTAC |
| 21 | G W V L | D L Q | E A P | A A D E | L S S | G K M |
| 121 | GCAGAGACTG | GAAGGACCTG | GAAGCCCCAT | CAGGGTAACA | ACAATGTCCG | CCTTCCAAGA |
| | CGTCTCTGAC | CTTCCTGGAC | CTTCGGGGTA | GTCCCATTGT | TGTTACAGGC | GGAAGGTTCT |
| 41 | A E T G | R T W | K P H | Q G N N | N V R | L P R |
| 181 | GCCTTACCTG | GTTTGTGCCG | GCTGTGGAGC | CTGACCCTAC | CAGTGGCTGA | GCTTGGCCTG |
| | CGGAATGGAC | CAAACACGGC | CGACACCTCG | GACTGGGATG | GTCACCGACT | CGAACCGGAC |
| 61 | A L P G | L C R | L W S | L T L P | V A E | L G L |
| 241 | GGCTATGCCT | CAGAGGAGAA | GATTATCTTC | CGATACTGTG | CTGGCAGCTG | TCCCCAAGAG |
| | CCGATACGGA | GTCTCCTCTT | CTAATAGAAG | GCTATGACAC | GACCGTCGAC | AGGGGTTCTC |
| 81 | G Y A S | E E K | I I F | R Y C A | G S C | P Q E |
| 301 | GTCCGTACCC | AGCACAGTCT | GGTGCTGGCC | CGTCTTCGAG | GGCAGGGTCG | AGCTCATGGC |
| | CAGGCATGGG | TCGTGTCAGA | CCACGACCGG | GCAGAAGCTC | CCGTCCCAGC | TCGAGTACCG |
| 101 | V R T Q | H S L | V L A | R L R G | Q G R | A H G |
| 361 | AGACCTTGCT | GCCAGCCAC | CAGCTATGCT | GATGTGACCT | TCCTTGATGA | CCACCACCAT |
| | TCTGGAACGA | CGGTCGGGTG | GTCGATACGA | CTACACTGGA | AGGAACTACT | GGTGGTGGTA |
| 121 | R P C C | Q P T | S Y A | D V T F | L D D | H H H |
| 421 | TGGCAGCAGC | TGCCTCAGCT | CTCAGCCGCA | GCTTGTGGCT | GTGGTGGCTG | A |
| | ACCGTCGTCG | ACGGAGTCGA | GAGTCGGCGT | CGAACACCGA | CACCACCGAC | T |
| 141 | W Q Q L | P Q L | S A A | A C G C | G G | . |

Figure 18B

PCB6
Rat PSP
Murine PSP
COS cell lysate
Mature PSP (E.coli)

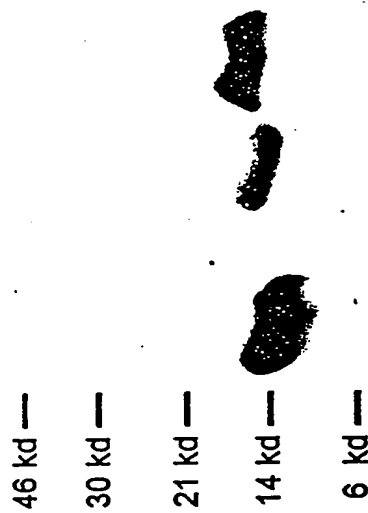


Figure 19

FIGURE 20A

PSP/NTN (SEQ ID NO:137)

ALAGSCLWSLTLPVAELGLGYASEEKVIFRYCAGSCPQEARTQHSLVLA 50
↓
RLRGRGRAHGRPCCRPTAYEDEVSFLDVHSRYHTLQELSARECACV 96

FIGURE 20B

NTN/PSP (SEQ ID NO:142)

PGARPCGLRELEVRVSELGLGYTSDETVLFRYCAGACEAAIRIYDLGLRR 50
↓
LRQRRRVRRERARAHPCQCPTSADVTFLDDQHHWQQLPQLSAAACGCGG 100

This is a high-contrast, black-and-white image showing a dense, textured surface. The image is heavily speckled and noisy, with many small, bright, circular features scattered across a dark background. These features appear as bright white or light gray spots, some of which are more distinct and circular than others. The overall texture is grainy and irregular, suggesting a microscopic view of a material or a close-up of a rough surface. The lighting is very high, creating a stark contrast between the dark background and the bright spots.

Figure 21a



Figure 21b

TOH labeled cells in E14 mesencephalic cultures

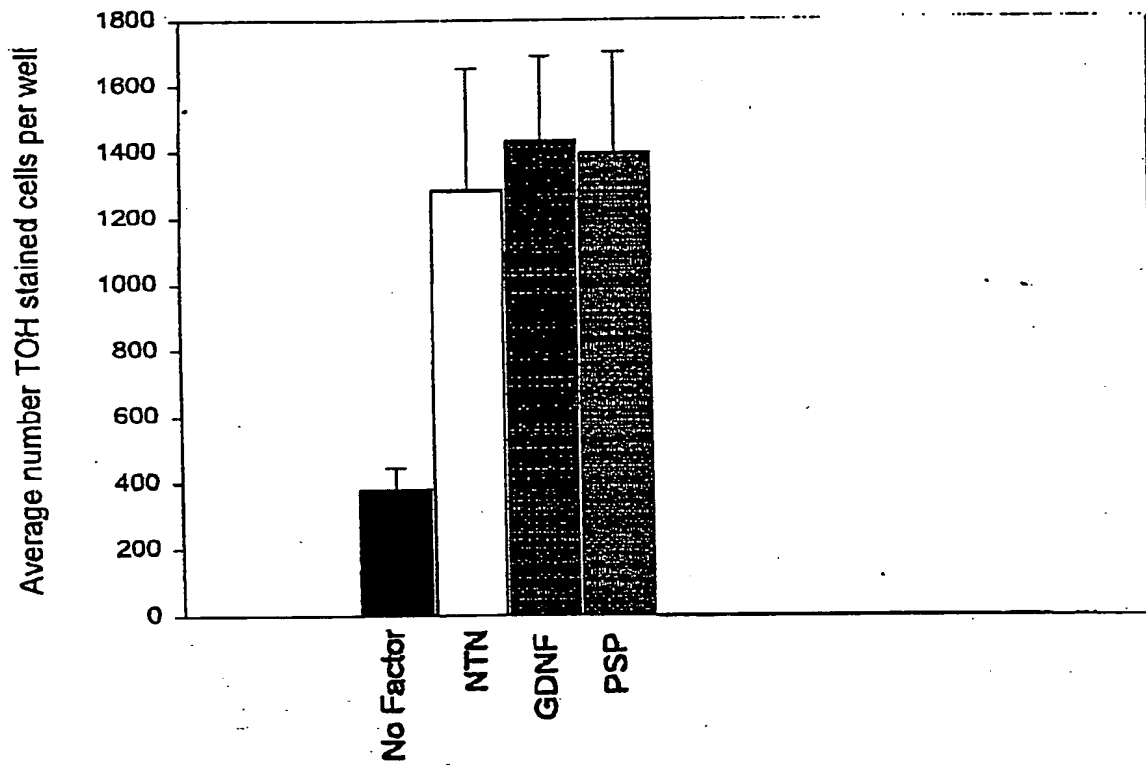


Figure 22

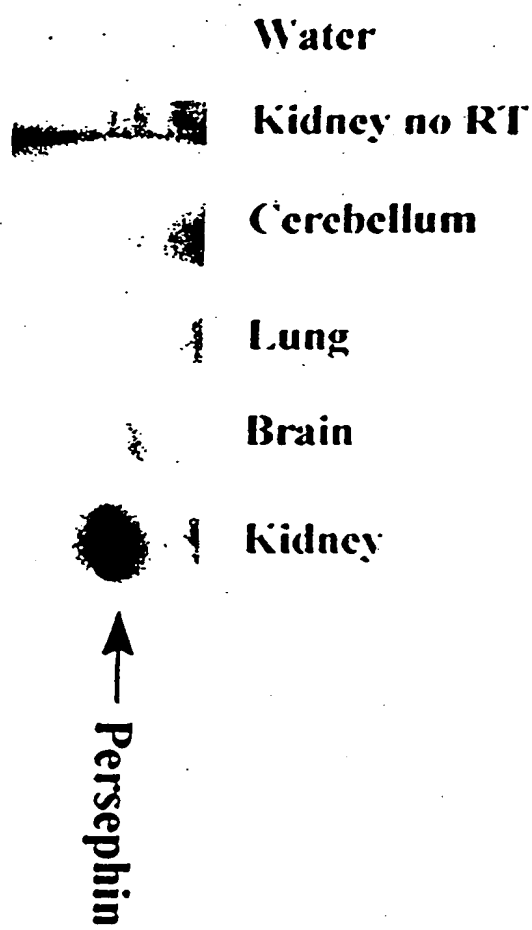


Figure 23

